IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
Pantoliano *et al.*	Art Unit: To be Assigned
Appl. No. To be Assigned (Continuation of Appl. No. 09/190,128)	Examiner: To be Assigned
Filed: Herewith	Atty. Docket: 1503.0310002/JAG/CMB
For: **High Throughput Method for Functionally Classifying Proteins Identified Using a Genomics Approach**	

Preliminary Amendment

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination on the merits, kindly amend the captioned application as follows.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments

In the Specification:

Please substitute the paragraph beginning on page 1, line 5, with the following paragraph:

The present invention claims priority benefit of U.S. nonprovisional Appl. No. 09/190,128, filed November 12, 1998 and U.S. provisional Appl. No. 60/065,129, filed November 12, 1997, both of which are hereby incorporated by reference in their entirety.

In the Claims:

Please cancel claims 1-30 without prejudice or disclaimer.

Please add the following new claims::

31. (New) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules for their ability to modify the stability of a target protein, wherein modification of the stability of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a first list of molecules that modify the stability of said target protein;

(c) comparing said first list from step (b) to at least one second list of molecules, wherein said second list of molecules are known to modify the stability of a group of proteins which share biological function; and

(d) determining if any molecule in said first list from step (b) is included in said second list from step (c), thereby determining at least one previously unidentified biological function of said target protein.

32. (New) The method of claim 31, wherein said screening step (a) comprises:

(a1) contacting said target protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) treating said target protein in each of said multiplicity of containers to cause said target protein to unfold;

(a3) measuring in each of said containers a physical change associated with the unfolding of said target protein;

(a4) generating an unfolding curve for said target protein for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other unfolding curves and to (2) the unfolding curve obtained for said target protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules modifies the stability of said target protein, wherein a modification in stability is indicated by a change in said unfolding curve.

33. (New) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules known to bind to a first list of molecules for their ability to modify the stability of a target protein, wherein said first list of molecules are known to modify the stability of a group of proteins which share biological function, and wherein modification of the stability of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a second list of molecules that modify the stability of said target protein;

(c) determining if any molecule in said first list from step (a) is included in said second list from step (b), thereby determining at least one previously unidentified biological function of said target protein.

34. (New) The method of claim 33, wherein said screening step (a) comprises:

(a1) contacting said target protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) treating said target protein in each of said multiplicity of containers to cause said target protein to unfold;

(a3) measuring in each of said containers a physical change associated with the unfolding of said target protein;

(a4) generating an unfolding curve for said target for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other unfolding curves and to (2) the unfolding curve obtained for said target protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules modifies the stability of said target protein, wherein a modification in stability is indicated by a change in said unfolding curve.

35. (New) A method for determining at least one previously unidentified biological function of a target protein comprising:

determining at least one previously unidentified biological function of said target protein if molecules that modify the stability of said target protein modify the stability of proteins which share biological function.

36. (New) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules for their ability to shift the thermal unfolding curve of a target protein, wherein a shift the thermal unfolding curve of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a first list of molecules that shift the thermal unfolding curve of said target protein;

(c) comparing said first list from step (b) to at least one second list of molecules, wherein said second list of molecules are known to modify the stability of a group of proteins which share biological function; and

(d) determining if any molecule in said first list from step (b) is included in said second list from step (c), thereby determining at least one previously unidentified biological function of said target protein.

37. (New) The method of claim 36, wherein said screening step (a) comprises:

(a1) contacting said protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) heating said multiplicity of containers from step (a1);

(a3) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(a4) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other thermal unfolding curves and to (2) the thermal unfolding curve obtained for said protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said protein.

38. (New) The method of claim 37, wherein said comparing step (a5) comprises ranking said molecules in said multiplicity of different molecules for said target protein according to the ability of each of said multiplicity of different molecules to shift the thermal unfolding curve of said target protein.

39. (New) The method of claim 37, wherein in said heating step (a2), said multiplicity of containers is heated simultaneously.

40. (New) The method of claim 37, wherein said step (a4) further comprises determining a midpoint temperature (T_m) from the thermal unfolding curve; and

wherein said step (a5) further comprises comparing the T_m of each of said unfolding curves in step (a4) to (1) the T_m of each of said other thermal unfolding curves and to (2) the T_m of the thermal unfolding curve obtained for said target protein in the absence of any of said different molecules.

41. (New) The method of claim 37, wherein said step (a3) comprises measuring the absorbance of light by said contents of each of said containers.

42. (New) The method of claim 37, wherein said step (a1) comprises contacting said target protein with a fluorescence probe molecule present in each of said multiplicity of containers and wherein said step (a3) comprises

(i) exciting said fluorescence probe molecule, in each of said multiplicity of containers, with light; and

(ii) measuring the fluorescence from each of said multiplicity of containers.

43. (New) The method of claim 42, wherein said step (a3)(ii) further comprises measuring the fluorescence from each of said multiplicity of containers one container at a time.

44. (New) The method of claim 42, wherein said step (a3)(ii) further comprises measuring the fluorescence from a subset of said multiplicity of containers simultaneously.

45. (New) The method of claim 42, wherein said step (a3)(ii) further comprises measuring the fluorescence from each of said multiplicity of containers simultaneously.

46. (New) The method of claim 37, wherein said step (a3) comprises

(i) exciting tryptophan residues in said target protein, in each of said multiplicity of containers, with light; and

(ii) measuring the fluorescence from each of said multiplicity of containers.

47. (New) The method of claim 37, wherein said multiplicity of containers in step (a1) comprises a multiplicity of wells in a microplate.

48. (New) A method for determining at least one previously unidentified biological function of a target protein comprising:

(a) screening a multiplicity of different molecules known to bind to a first list of molecules for their ability to shift the thermal unfolding curve of a target protein, wherein said first list of molecules are known to modify the stability of a group of proteins which share biological function, and wherein a shift in the thermal unfolding curve of said target protein by a molecule indicates that the molecule binds to said target protein;

(b) generating, from step (a), a second list of molecules that modify the stability of said target protein;

(c) determining if any molecule in said first list from step (a) is included in said second list from step (b), thereby determining at least one previously unidentified biological function of said target protein.

49. (New) The method of claim 48, wherein said screening step (a) comprises:

(a1) contacting said protein with one or more of said multiplicity of different molecules in each of a multiplicity of containers;

(a2) heating said multiplicity of containers from step (a1);

(a3) measuring in each of said containers a physical change associated with the thermal unfolding of said target molecule resulting from said heating;

(a4) generating a thermal unfolding curve for said target molecule as a function of temperature for each of said containers; and

(a5) comparing each of said unfolding curves in step (a4) to (1) each of said other thermal unfolding curves and to (2) the thermal unfolding curve obtained for said protein in the absence of any of said multiplicity of different molecules; and

(a6) determining whether any of said multiplicity of different molecules shift the thermal unfolding curve of said protein.

50. (New) The method of claim 49, wherein said comparing step (a5) comprises ranking said molecules in said multiplicity of different molecules for said target protein according to the ability of each of said multiplicity of different molecules to shift the thermal unfolding curve of said target protein.

51. (New) The method of claim 49, wherein in said heating step (a2), said multiplicity of containers is heated simultaneously.

52. (New) The method of claim 49, wherein said step (a4) further comprises determining a midpoint temperature (T_m) from the thermal unfolding curve; and

wherein said step (a5) further comprises comparing the T_m of each of said unfolding curves in step (a4) to (1) the T_m of each of said other thermal unfolding curves and to (2) the T_m of the thermal unfolding curve obtained for said target protein in the absence of any of said different molecules.

53. (New) The method of claim 49, wherein said step (a3) comprises measuring the absorbance of light by said contents of each of said containers.

54. (New) The method of claim 49, wherein said step (a1) comprises contacting said target protein with a fluorescence probe molecule present in each of said multiplicity of containers and wherein said step (a3) comprises

(i) exciting said fluorescence probe molecule, in each of said multiplicity of containers, with light; and

(ii) measuring the fluorescence from each of said multiplicity of containers.

55. (New) The method of claim 54, wherein said step (a3)(ii) further comprises measuring the fluorescence from each of said multiplicity of containers one container at a time.

56. (New) The method of claim 54, wherein said step (a3)(ii) further comprises measuring the fluorescence from a subset of said multiplicity of containers simultaneously.

57. (New) The method of claim 54, wherein said step (a3)(ii) further comprises measuring the fluorescence from each of said multiplicity of containers simultaneously.

58. (New) The method of claim 49, wherein said step (a3) comprises

(i) exciting tryptophan residues in said target protein, in each of said multiplicity of containers, with light; and

(ii) measuring the fluorescence from each of said multiplicity of containers.

59. (New) The method of claim 48, wherein said multiplicity of containers in step (a1) comprises a multiplicity of wells in a microplate.

60. (New) A method for determining at least one previously unidentified biological function of a target protein comprising:

determining at least one previously unidentified biological function of said target protein if molecules that shift the thermal unfolding curve of said target protein shift the thermal unfolding curves of proteins which share biological function.

Remarks

Upon entry of the foregoing amendment, claims 31-60 are pending in the application. New claims 31-60 are sought to be added. These changes are believed to introduce no new matter, and their entry is respectfully requested.

The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375 (Fed. Cir. 1983). The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. M.P.E.P. § 2163.02.

The specification clearly indicates that the inventors were in possession of the claimed invention. Specifically, support for new claims 31-60 is found in the originally filed claims and in the specification at page 10, lines 18-21, which state that functionally classifying proteins refers to classifying a protein according to a biological, biochemical, physical or chemical function. Support for the new claims is also found at page 13, lines 21-24 of the specification which state that the invention can confirm, reject or elaborate a hypothesized function of the target protein. Further support is found at page 21, lines 12-16 of the specification, which state that the invention encompasses determining a previously unknown function of a protein of previously known function. Support for the amendment of the claims is also found in the specification at page 11, line 14; page 12, lines 19-21; page 21, line 2; page 24, lines 25-26; page 25, lines 3-9; page 31, lines 17-20

and 28-30; page 32, line 22; page 34, line 15 to page 35, line 5. No new matter will be added by this amendment.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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